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ORIGINAL ARTICLE

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ABSTRACT

BACKGROUND: Methylsulfonylmethane (MSM) has been shown to have antioxidant and anti-inflammatory properties, which may attenuate exercise-induced oxidative stress and muscle soreness. We determined the impact of MSM on exercise-induced oxidative stress, muscle soreness, and muscle function.

METHODS: Forty physically active (*i.e.*, exercise-trained) men were assigned in double-blind manner to placebo (N.=20) or MSM (3 grams per day; N.=20) for 28 days before performing 10 sets of 10 repetitions of eccentric knee extension exercise. Functional capacity and muscle soreness was evaluated before and through 72 hours post-eccentric exercise, and both urine and blood were collected for determination of oxidative stress.

RESULTS: Exercise resulted in impairment in muscle function and an increase in muscle soreness. Oxidative stress biomarkers were largely unaffected by exercise, perhaps due to the trained nature of the subjects. Although not of statistical significance, MSM supplementation attenuated muscle soreness by approximately 15-20% and allowed for a more rapid recovery of isometric quadriceps force (*i.e.*, values returned to baseline by 72 hours post exercise for MSM but remained 8% below baseline for placebo). No other differences were noted between MSM and placebo.

CONCLUSIONS: Four weeks of MSM supplementation provides some degree of muscle protection following exercise, with regards to muscle force production and soreness. Considering that oxidative stress was not increased in response to exercise, MSM supplementation does not appear necessary for purposes of decreasing oxidative stress following exercise, at least as performed by physically active men.

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Key words: Reactive oxygen species - Exercise - Dietary supplements - Dimethyl sulfone.

Eccentric exercise involves muscle contractions that occur while the muscle is actively lengthening, and has been known for many years to cause low-grade muscle damage.[1] This muscle damage occurs to some extent in most individuals each time they exercise, in particular when the exercise is vigorous. In a laboratory setting, controlled and relatively high volume eccentric exercise is often used to induce acute skeletal muscle damage.[2, 3] These laboratory-controlled muscle damage protocols are often designed to study the impact of various interventions aimed at reducing the degree of damage, or speeding up the recovery process following strenuous exercise.

To better understand the degree of muscle

injury and functional impairment, investigators have compared maximal contraction forces and associated variables (*e.g.*, counter-movement jump power), both before and following exercise bouts. For example, maximal isometric force [4] and counter-movement vertical jump (CMVJ) power have been shown to decrease immediately following eccentric knee extensor exercise [5] and remain below pre exercise values for several days post exercise. Delayed onset muscle soreness (DOMS) is apparent post exercise, possibly being one cause of the individual's reduction in force generation due to increased soreness within the muscle.

Although the majority of muscle injury appears to be mechanical in nature (*i.e.*, the muscle fibers are elongated and undergo slight tearing),[6] the degree of injury appears compounded by the post exercise elevation in reactive oxygen species (ROS).[7] Increased ROS (also referred to as "free radicals") can degrade proteins and lipids and cause further impairments in physical performance.[8, 9] Increased ROS promote a condition referred to as "oxidative stress". This oxidative stress is associated with elevated inflammation during the hours and days following muscle injury [10, 11] and the inflammation can increase the perceived level of muscle pain or soreness.[12] Identifying methods of reducing oxidative stress, inflammation, and associated symptoms of muscle injury is of interest to scientists, coaches, and athletes.

Methylsulfonylmethane (MSM) is widely used as a dietary supplement and has been reported to lessen ROS production [13] and to have anti-inflammatory activity.[14, 15] This is true with regards to exercise producing oxidative stress and/or muscle soreness.[16-18] In these studies, subjects received daily MSM dosages of 50 mg/kg (approximately 4 grams). While MSM has been reported to attenuate oxidative stress following strenuous exercise, limited data are available on the role of MSM supplementation to attenuate the typically observed muscle force production and physical performance impairments following eccentric exercise-induced muscle damage.

The present study was designed to determine the influence of MSM on oxidative stress, muscle soreness, muscle force production and physical performance following isolated eccentric knee extensor exercise in physically active men. It was hypothesized that MSM would attenuate oxidative stress, while resulting in a lesser degree of muscle force production and physical performance impairment following eccentric exercise compared to a placebo treatment.

Materials and methods

A target of 40 men was planned for this study in order to have adequate statistical power, using 8-isoprostanes as the dependent variable in the power calculation. Fifty-four healthy men were recruited and provided informed consent to participate in this study but fourteen of these men failed to complete all aspects of this study. Therefore, their data were not included in the analysis. Some men withdrew from the study before any testing had begun, while others began testing and needed to withdraw due to personal reasons (*e.g.*, moving from area, time commitments). Therefore, a total of 40 men began the study and completed testing (Table I). Women were not enrolled in this study, as hormonal changes across the menstrual cycle could have influenced our outcome measures.[19-21]

TABLE I.—*Descriptive characteristics of 40 men assigned to either placebo or MSM for four weeks.*

Variable	Placebo (N.=20)	MSM (N.=20)
Age (years)	25.5±1.2	25.1±1.6
Height (cm)	178.8±1.5	176.5±1.4
Weight (kg)	83.6±2.4	84.6±1.5
BMI (kg·m^{-2})	26.1±0.6	27.2±0.5
Waist/hip ratio	0.87±0.01	0.86±0.01
Heart rate (bpm)	69.6±2.1	65.9±1.8
Systolic blood pressure (mmHg)	123.6±2.1	119.9±1.7
Diastolic blood pressure (mmHg)	80.5±1.8	78.2±1.7
Knee extensor 1RM (kg)	147.2±4.1	151.9±5.6
Years anaerobic exercise training	6.0±1.1	7.1±1.6
Hours per week anaerobic exercise	4.0±0.6	4.7±0.5
Years aerobic exercise training	6.2±1.1	7.2±1.8
Hours per week aerobic exercise	3.4±0.7	2.2±0.3
Compliance to capsule intake (%)	96.2±1.4	96.6±1.0

Data are presented as mean±SEM.
No statistically significant differences were noted (P>0.05).

Subjects were not current smokers and did not have any cardiovascular/metabolic disorders (*e.g.*, hypertension, diabetes) or musculoskeletal injuries. Subjects were not obese based on body mass index standards (<30 kg/m^2), as obese individuals often present with elevated levels of oxidative stress [22] and inflammation.[23] Health history, medication and dietary supplement usage, and physical activity questionnaires were completed by all subjects to determine eligibility. All subjects had performed resistance exercise for a minimum 6 months prior to beginning the study, with at least one session per week of lower body resistance exercise. This was to provide adequate adaptations to the skeletal, muscular, and neuromuscular systems, all of which were heavily taxed when performing the exercise test battery as a component of this study. Using sedentary subjects would have been problematic, due to the well-described repeated bout effect of routine exercise.[24] Moreover, as MSM is typically used by those who are physically active, using sedentary subjects may not have allowed for data to be generalized to a more active population.

Subjects were not using nutritional supplements that were thought to affect the outcome measures (such as antioxidants or anti-inflammatory agents), nor were they using non-steroidal anti-inflammatory drugs (NSAIDS) or other off-the-shelf or prescription agents that may have affected inflammation. If subjects were using any of the above agents upon screening, they were required to cease use at least three weeks prior to the start of testing. If subjects were using general dietary supplements (*e.g.*, multi-vitamin, protein powder), they were allowed to continue the same supplementation protocol throughout the study period. Prior to participation, each subject was informed of all procedures, potential risks, and benefits associated with the study through both verbal and written form in accordance with the procedures approved by The University of Memphis Institutional Review Board for Human Subjects Research (protocol #3006). Research was performed in compliance with the Helsinki Declaration. Subjects provided written informed consent prior to participating.

Design and supplementation

This study involved a double-blind, placebo-controlled design. Subjects were assigned to MSM (N.=20) or placebo (N.=20) capsules to ingest every day for a period of four weeks. Subjects were matched based on age and body mass in an effort to retain similarity between the MSM and placebo groups. Subjects continued ingesting their assigned treatment for the three days of exercise recovery (described below). It should be noted that one subject assigned to the MSM group supplemented for one additional week due to scheduling conflicts. Subjects ingested 3 capsules, once daily, for a total daily dosage of 3 grams of MSM. The MSM (OptiMSM®; Bergstrom Nutrition, Vancouver, WA, USA) and placebo (rice flour) capsules were produced according to Good Manufacturing Practice (GMP). Capsules were of similar appearance and provided to subjects in unlabeled bottles. Subjects returned their first capsule bottle at the end of week two of supplementation and a new bottle was provided. Remaining capsules were counted to determine compliance of capsule intake at the end of week 2 and week 4.

Screening lab visit

Following completion of informed consent and prior to beginning the assigned treatment, subjects reported to the lab for collection of anthropometric data. They were asked to empty their bladder and then rested for 10 minutes in a seated position. Following the rest period, technicians measured their heart rate (*via* 60-second palpation of radial artery) and blood pressure (*via* auscultation). Subjects' height was measured using a stadiometer, and their body weight was measured using a calibrated medical scale. Body mass index was calculated, and waist and hip circumference was measured using a tension-regulated tape. Subjects also completed a one-repetition maximum (1RM) test in the knee extension exercise and practiced all performance tests described be-

low. Within a few days of this session, subjects again reported to the lab to practice all performance tests one additional time — using the exact procedures as described below. This was necessary to minimize any potential learning effect of the exercise tests.

Eccentric exercise protocol

Subjects performed 10 sets of 10 eccentric-only repetitions (or repetitions to failure) of seated machine knee extension using approximately 100% of concentric one-repetition maximum. Investigators assisted the subjects in raising the weight to a level where the knees were fully extended. The subject then lowered the weight under control on a 4-second count (using a metronome set to one-second cues) to the ending position. Verbal reminders were given to keep the knees straight at the start of eccentric motion. Subjects were provided a 2-minute rest period between sets with this sequence being repeated for 10 sets. If the subject was unable to lower the weight over a 4-second count, the weight was reduced by approximately 10% for the subsequent sets, to keep the repetitions at 10 per set.

Testing procedures

Subjects reported to the lab a total of eight times, following the screening visit, as indicated below. The time of lab reporting was similar for each subject on all days (with the possible exception of visit 1).

1. Familiarization trials for all exercise tests (no blood collection)
2. Pre supplementation: baseline 1 assessment (data collection)

Supplementation period: 14 days

3. Mid supplementation assessment: blood collection only

Supplementation period: 14 days

4. Post supplementation: Baseline 2 assessment (data collection)
5. Induce acute muscle injury (eccentric exercise) followed by immediate data collection
6. 24 hour data collection
7. 48 hour data collection
8. 72 hour data collection.

Subjects may have reported to the lab at any time of day to perform the familiarization trials. However, for all other visits, subjects reported to the lab in a 10-hour fasted state, during the morning hours (6:00-10:00 a.m.). Upon arrival to the lab on each day, subjects rested quietly for 20 minutes (after providing investigators with any needed information or collected urine—on appropriate days as indicated below). Specific to collected urine, subjects were required to collect urine samples during the 24 hours prior to visits #2, 4, 6, 7, and 8. This was done by voiding into a standard urine collection container. The collection container was then turned in to an investigator upon arrival to the lab.

A venous blood sample (~20 mL; 4 teaspoons) was obtained from a forearm vein. For visits #2, 4, 5, 6, 7, and 8, subjects had blood collected and performed exercise testing. On visit 5, blood was collected immediately following the eccentric exercise protocol. Subjects also completed questionnaires related to their degree of muscle soreness and level of fatigue (visual analog scale). After blood was collected on these days, subjects received a standard liquid meal containing orange juice and vanilla protein powder (approximately 225 calories). We have used this same meal in previous studies and it is well-tolerated and enjoyed by most subjects. Subjects then rested for 15-20 minutes and exercise testing began.

Performance testing

Testing was completed once per day on five consecutive days (days 4-8 above). On the second day, the eccentric exercise protocol was completed first, followed directly by all other laboratory tests. All tests were completed as quickly as possible without compromising data collection procedures, in order to limit recovery time. The order of tests, without consideration of the intervention of eccentric exercise, are as follows: maximal voluntary isometric knee extensor force (MIF), countermovement vertical jump (CMVJ), timed 20-yard running sprint, 30-second Wingate cycle

anaerobic power test, and a treadmill run test to exhaustion.

Maximum voluntary isometric knee extensor force

Following a 5-minute warm-up on a stationary bike, subjects were seated in a chair with their ankle attached to a cuff and cable with their shank hanging to allow a passive knee angle. The knee angle was controlled to 90 degrees using a goniometer while the cable was under tension. A load cell (Model MLP-1K, Transducer Techniques, Temecula, CA, USA) was attached to the cable in series for measuring isometric force. Subjects were asked to place their arms over their chest, to keep the left leg relaxed, and not swing their leg just before the maximum contraction. Subjects were then asked to push maximally against the cuff (the cuff did not move) on a verbal command for three to four seconds, and then asked to relax. Two practice trials were completed at 50% and 85% maximum effort, respectively. Three maximal trials were then completed. Rest periods of one to two minutes were given between all trials. The Datapac 5 software (RUN Technologies, Mission Viejo, CA) was used to compute the maximal knee extensor force from three trials. Data were collected at 2 kHz and filtered with a 4th order, low-pass Butterworth filter (20-Hz cutoff). The highest peak value during the entire trial was taken as the MIF, with the mean plateau of force (*i.e.*, value obtained during the force plateau phase) taken as the MIF plateau.

Countermovement vertical jump

Subjects completed three CMVJs for maximal height. Practice trials were given until the subject felt comfortable with the motion. Subjects were instructed to use a countermovement to a self-selected depth with arm swing. Vertical jump displacement was measured using a stand-alone Vertec™ jump trainer. Jump displacement was measured to the nearest 1.27 cm, calculated as jump height minus one-hand reach height from a static, plantar-flexed position.

20-yard running sprint

The running sprint was preceded by light stretching. Subjects then performed two maximal efforts sprints, with approximately two minutes between sprints. The test required subjects to run as fast as possible over a 20-yard distance. The run time was measured by hand with a stopwatch to the 0.1 second. The same researcher timed the run for all subjects and the best of the two run times was used for data analysis. The subject was provided with a queue by the researcher to begin the sprint and the researcher was stationed at the finish line to record the sprint time.

Wingate cycle anaerobic power test

An assessment of anaerobic power was performed using a short duration (30-second), Wingate cycle sprint test performed on a computer-interfaced, friction resisted cycle ergometer (Monark Ergomedic 894E, Vansbro, Sweden). Initially, subject's seat height was adjusted so that at full extension (six o'clock on crank) there was a slight bend (~10 degrees) at the knee, and the setting was recorded for subsequent sessions. Subjects were required to perform a 5-minute warm-up at minimal resistance (~1 kg) incorporating two brief (3-5 seconds) pre-starts. Pre-starts were used in order to ensure that subjects were familiar with required sprinting techniques. Upon commencement of test protocol, subjects were instructed to begin an all-out sprint against no resistance until 150 revolutions per minute (RPM) was reached and a RPM plateau was obtained, after which time the designated load (0.075 kg per kg of subject's body mass) was automatically applied. Upon completion of the test protocol, subjects were instructed to pedal against very light resistance (1 kg) for a 3-5 minute period.

Treadmill run test to exhaustion

On visits #2, 4, and 8 only, aerobic running performance was assessed on a treadmill using a previously described protocol,[25] which increases in speed or grade every two minutes.

Heart rate (via heart rate monitors) and perceived exertion (using the Borg Scale of 1-10) were measured at minutes 8 and 14 to confirm the level of exertion, as well as at the conclusion of testing.

Muscle soreness and fatigue

Using a 10-point scale, subjects were asked to rate their quadriceps muscle soreness during maximal squatting and passive knee extensor stretching (*i.e.*, knee flexion). Subjects were lying supine with their hips flexed at 90 degrees. A researcher passively flexed the knee by moving the leg towards the thigh until maximum flexion was reached. Subjects were also asked to rate their overall fatigue using a 10-point scale (0 for no soreness/fatigue; 10 for very, very sore/fatigued).

Blood and urine collection and analysis

At each collection time indicated above, a venous blood sample (~20 mL; 4 teaspoons) was obtained from a forearm vein. Blood collected in tubes containing EDTA was centrifuged immediately at 4 °C and plasma was stored in multiple aliquots at -70 °C until analyzed. Blood collected in tubes with no additive was allowed to clot at room temperature for 30 minutes and then centrifuged at 4 °C. The serum was stored in multiple aliquots at -70 °C until analyzed.

Malondialdehyde (MDA) was analyzed in plasma using a commercially available colorimetric assay (Northwest Life Science Specialties, Vancouver, WA, USA; NWK-MDA01), using methods similar to those previously described.[26] The coefficient of variation for MDA was 3.6%. Advanced oxidation protein products (AOPP) were analyzed in plasma using a commercially available assay (Cell Biolabs, Inc., San Diego, CA, USA; STA-318). The coefficient of variation for AOPP was 2.8%. Oxidized low-density lipoprotein (LDL) [oxLDL] was analyzed in serum using a commercially available enzyme linked immunosorbent assay (Alpco Diagnostics, Salem, NH; 30-7810). The coefficient of variation for oxLDL was 9.1%. Values for MDA, AOPP, and oxLDL were quantified using a Bio-Tek (Winooski, VT, USA) microplate reader and Gen5 software. All assayed were performed in duplicate on first thaw. Urine samples (aliquot from the 24 hour collected sample) were used for the analysis of 8-isoprostanes using gas chromatography-mass spectrometry techniques, according to the methods described by Milne *et al.*[27] Values are expressed in nanograms per milligram of creatinine.

Dietary intake and physical activity

All subjects were instructed to consume their usual diet throughout the study period, with the following exception: Food intake was standardized during the day before each data collection day (day 2; days 4-8). As we have done in past studies, subjects received prepackaged meal replacement drinks and bars, along with nuts and fruit to consume each day. Subjects were provided with ample food so that in most cases they ate as much as desired. The daily ration included 4 "ready-to-drink" meal replacement shakes (~250 kcal each), 4 meal replacement bars (~200 kcal each), one package of nuts (~200 kcal), and 4 pieces of fresh fruit (apples and bananas). This provided subjects with approximately 2500 kcal per day. Subjects were instructed not to consume any other food or beverages, aside from water, during the days prior to each test day. Subjects were instructed not to consume alcohol or caffeinated beverages (such as "energy drinks", coffee, tea, or soda) or dietary supplements containing caffeine or other stimulants, during the two days prior to each test day. Subjects were instructed not to engage in any strenuous physical activity during the two days before exercise testing (pre and post intervention) and during the entire week following the eccentric exercise protocol (during which time data collection was taking place).

Statistical analysis

Data were analyzed using a 2×5 (group × time) repeated measures analysis of

variance (RMANOVA), using data obtained from pre-exercise (baseline 2 only) and all post-exercise times. Tukey's *post-hoc* tests were used as needed. Percent change values from pre-exercise (baseline 2) were calculated for biochemical and performance variables and analyzed using RMANOVA. Baseline 1 and baseline 2 values were compared using a one-way ANOVA. Statistical significance for all tests was set *a priori* at $P \leq 0.05$.

Results

Compliance to capsule intake was approximately 96% for subjects in both groups (Table I). Compliance was further confirmed by an analysis of blood MSM — the subject of a separate manuscript.[29]

Adverse events

Four adverse events were reported during the course of the study period. None of these appeared to be associated with the use of MSM or placebo capsules. One subject experienced a skin rash, likely due to the skin preparation necessary as part of the biomechanical testing procedures. The remaining three adverse events were associated with the exercise testing. Specifically, one subject fainted after performing the Wingate cycle test, one subject experienced knee pain as a result of performing the eccentric exercise protocol, and one subject appeared to tear his hamstring muscle as he was completing the 20 yard sprint. All of these subjects continued in the study, with the exception of the subject who experienced knee pain as a result of performing the eccentric exercise protocol. The subject who appeared to tear his hamstring did so during his last day of testing. Therefore, all data for this subject are available except for his final Wingate test and treadmill test.

Missing data

There were some missing data associated with the study. Regarding biochemical measures, these are as follows: for MDA and AOPP, one sample for the immediate post-exercise time is not included for one subject assigned to placebo. For oxLDL, values were not available for two subjects in the MSM group and two subjects in the placebo group (all values were below the low standard used in the assay).

Regarding the performance measures, Wingate data at the Baseline 1 time is not included for one subject assigned to placebo and one subject assigned to MSM. In addition, Wingate data at 72 hours post-exercise are not available for one subject assigned to MSM (the subject who appeared to tear his hamstring). Treadmill time is not available at the baseline 1 time for one subject assigned to placebo and for 72 hours post-exercise for two subjects assigned to MSM.

Subject characteristics and baseline values

Subject descriptive characteristics were not different between MSM and placebo ($P>0.05$) (Table I). A comparison from Baseline 1 to Baseline 2 noted no significance differences across time ($P>0.05$) for any biochemical or performance variable. Although small differences were noted between groups with regards to certain baseline 1 and baseline 2 values, Tukey's *post-hoc* analysis indicated no significant differences between groups ($P>0.05$). Data for all time points of collection (baseline 1, baseline 2, immediately post-exercise, and at 24, 48, and 72 hours post-exercise) are included within the tables for comparison purposes.

Biochemical measures

With regards to the blood and urinary oxidative stress biomarkers (Table II), the following was noted: A group effect was noted for MDA ($P=0.04$; $r=0.14$), with values lower for MSM compared to placebo. No time effect ($P=0.47$) or interaction effect ($P=0.65$) was noted. A group effect was noted for AOPP ($P=0.05$; $r=0.14$), with values lower for MSM compared to placebo. No time effect ($P=0.36$) or interaction effect ($P=0.98$) was noted. A group effect

TABLE II.—*Blood and urinary oxidative stress biomarker data of 40 men assigned to either placebo or MSM for four weeks.*

Biomarker	Group	Baseline 1	Baseline 2	0 hours post	24 hours post	48 hours post	72 hours post
MDA (μmol/L)*	Placebo	0.65±0.05	0.64±0.04	0.59±0.03	0.55±0.03	0.60±0.03	0.59±0.03
	MSM	0.58±0.03	0.57±0.04	0.57±0.03	0.56±0.03	0.53±0.03	0.52±0.02
AOPP (μmol/L)*	Placebo	18.2±2.2	16.4±1.5	15.8±1.2	14.6±1.7	16.2±1.4	14.5±1.3
	MSM	13.3±1.0	14.4±1.5	15.2±1.1	13.2±0.7	14.2±1.7	12.3±0.6
oxLDL (μmol/L)*	Placebo	324.9±76.0	348.1±76.4	317.9±75.6	303.8±71.1	293.8±67.2	304.0±69.7
	MSM	155.0±34.5	214.9±69.4	241.9±77.0	204.4±69.1	198.6±82.4	184.3±67.7
8-iso (ng/mgCr)* ‡	Placebo	1.41±0.13	1.27±0.10	NA	1.18±0.11	1.10±0.10	1.12±0.15
	MSM	1.02±0.11	1.05±0.1	NA	0.99±0.10	1.05±0.11	0.87±0.07

Values are presented as mean ± SEM.
*Condition effect for MDA (P=0.04), AOPP (P=0.05), oxLDL (P=0.02), and 8-iso (P=0.03); ‡ values obtained in urine samples.
No other statistically significant effects noted (P>0.05)

TABLE III.—*Physical performance measures of 40 men assigned to either placebo or MSM for four weeks.*

Performance test	Group	Baseline 1	Baseline 2	0 hours post	24 hours post	48 hours post	72 hours post
MIF peak (N)* †	Placebo	555.3±26.6	541.0±22.8	422.4±23.8	483.0±25.4	502.4±26.4	500.2±27.5
	MSM	636.6±31.1	604.6±32.9	478.5±33.0	528.2±34.0	559.8±38.0	595.0±39.3
MIF plateau (N)* †	Placebo	495.3±25.4	486.5±23.7	362.9±24.3	432.7±25.3	450.7±26.2	449.1±27.9
	MSM	549.9±28.7	531.8±31.5	410.5±31.4	465.0±32.1	508.9±37.0	529.7±38.8
Vertical jump (in)* †	Placebo	17.9±1.0	18.0±0.8	15.2±1.0	15.9±0.8	16.1±0.8	16.5±0.7
	MSM	20.8±1.0	20.3±0.9	17.8±0.9	18.7±0.9	18.7±0.9	19.0±0.8
20 yard sprint (s)* †	Placebo	3.31±0.04	3.32±0.06	3.71±0.23	3.60±0.15	3.49±0.11	3.37±0.08
	MSM	3.14±0.06	3.15±0.05	3.38±0.07	3.33±0.08	3.30±0.06	3.18±0.07
Wingate PP (W/kg) †	Placebo	11.7±0.8	10.9±0.4	9.9±0.3	10.2±0.3	10.1±0.2	10.2±0.3
	MSM	11.5±0.4	11.0±0.3	10.0±0.3	10.1±0.3	10.6±0.3	10.4±0.3
Wingate work (W/kg)	Placebo	237.4±6.3	237.3±4.6	225.8±6.6	234.2±5.4	234.3±4.9	236.1±5.5
	MSM	242.9±6.7	246.8±6.2	230.0±6.4	236.3±6.9	237.3±7.6	238.8±7.4

Values are presented as mean ± SEM.
MIF: maximal isometric force; Wingate PP: Wingate peak power.
*Condition effect for MIF (P=0.002), MIF plateau (P=0.006), vertical jump (P<0.0001), and 20 yard sprint (P=0.001); † time effect for MIF (P=0.002), MIF plateau (P=0.0008), vertical jump (P=0.05), 20-yard sprint (P=0.03), and Wingate peak power (P=0.02); values lower immediately post-exercise as compared to pre-exercise for MIF, vertical jump, and Wingate peak power; values higher for the 20-yard sprint.
No other statistically significant effects noted (P>0.05).

was noted for oxLDL (P=0.02; r=0.18), with values lower for MSM compared to placebo. No time effect (P=0.97) or interaction effect (P=0.99) was noted. A group effect was noted for 8-isoprostanes (P=0.03; r=0.23), with values lower for MSM compared to placebo. No time (P=0.55) or interaction (P=0.81) effect was noted.

Physical performance measures

A group effect was noted (Table III) for MIF (P=0.002), MIF plateau (P=0.006), vertical jump (P<0.0001), and 20-yard sprint (P=0.001). Values were higher for MSM compared to placebo for MIF and vertical jump, but lower (*i.e.*, faster) for the 20 yard sprint. A time effect was noted for MIF (P=0.002), MIF plateau (P=0.0008), vertical jump (P=0.05), 20 yard sprint (P=0.03), and Wingate peak power (P=0.02), with values lower immediately post-exercise as compared to pre-exercise for MIF, vertical jump, and Wingate peak power, but higher for the 20 yard sprint. No interaction effects were noted for any variable (P>0.05).

Maximal time, heart rate, and RPE during the treadmill test were not different between MSM and placebo or across time (P>0.05), with the exception of a group effect noted for maximum RPE (P=0.04), which was higher for MSM compared to placebo (Table IV).

Muscle soreness and fatigue

No group (P=0.46) or interaction (P=0.98) effect was noted for muscle soreness during

TABLE IV.—*Treadmill time and associated variables of 40 men assigned to either placebo or MSM for four weeks.*

Parameter	Group	Baseline 1	Baseline 2	72 hours post
Treadmill time (s)	Placebo	1193.1±44.6	1120.5±73.8	1143.1±58.2
	MSM	1234.0±45.4	1172.9±40.6	1249.6±40.3
HR min 8 (bpm)	Placebo	146.9±2.5	145.3±3.0	146.5±2.9
	MSM	145.6±3.3	146.8±3.1	145.1±3.7
RPE min 8 (1-10)	Placebo	4.1±0.3	4.6±0.3	4.8±0.4
	MSM	4.2±0.3	4.5±0.3	4.2±0.3
HR min 14 (bpm)	Placebo	164.3±3.1	165.4±3.9	166.0±2.6
	MSM	161.7±2.7	162.5±2.8	166.1±3.3
RPE min 14 (1-10)	Placebo	5.9±0.4	6.1±0.3	6.4±0.3
	MSM	5.7±0.5	6.5±0.4	6.5±0.3
HR max (bpm)	Placebo	183.5±3.5	176.0±5.2	182.7±2.3
	MSM	180.6±3.0	179.8±2.7	184.1±2.4
RPE max (1-10)*	Placebo	9.1±0.2	8.6±0.4	8.9±0.2
	MSM	9.1±0.2	9.1±0.2	9.5±0.1

Values are presented as mean ± SEM.
HR: heart rate; RPE: rating of perceived exertion.
*Condition effect for RPE max (P=0.04).
No other statistically significant effects noted (P>0.05).

TABLE V.—*Muscle soreness and fatigue ratings of 40 men assigned to either placebo or MSM for four weeks.*

Muscle soreness	Group	Baseline 1	Baseline 2	0 hours post	24 hours post	48 hours post	72 hours post
Squatting soreness*	Placebo	0.6±0.1	1.1±0.2	5.3±0.5	5.7±0.5	5.6±0.5	3.6±0.5
	MSM	0.6±0.2	0.7±0.4	4.9±0.4	5.6±0.4	5.7±0.6	3.5±0.6
Stretch soreness †	Placebo	0.3±0.2	0.4±0.2	3.4±0.6	6.2±0.4	6.2±0.4	4.4±0.4
	MSM	0.3±0.2	0.9±0.3	3.3±0.4	5.1±0.3	5.2±0.4	3.4±0.5
Fatigue §	Placebo	2.3±0.6	2.1±0.4	5.8±0.4	4.5±0.5	3.9±0.4	2.8±0.3
	MSM	1.8±0.3	1.8±0.2	4.5±0.3	3.8±0.4	3.7±0.4	2.9±0.5

Values are mean±SEM.
*Time effect for squatting soreness (P<0.0001); values higher than pre-exercise (baseline 2) at all times post-exercise; † time effect for stretching soreness (P<0.0001); values higher than pre-exercise (baseline 2) at all times post-exercise; § time effect for fatigue (P<0.0001); values higher than pre-exercise (baseline 2) immediately post-exercise, and at 24 hours and 48 hours post-exercise.
No other statistically significant effects noted (P>0.05).

squatting (Table V). However, a time effect was noted (P<0.0001), with values higher than pre-exercise at all times post-exercise. No group (P=0.07) or interaction (P=0.35) effect was noted for muscle soreness during passive stretch. However, a time effect was noted (P<0.0001), with values higher than pre-exercise at all times post-exercise. No group (P=0.07) or interaction (P=0.45) effect was noted for fatigue. However, a time effect was noted (P<0.0001), with values higher than pre-exercise immediately post-exercise, and at 24 and 48 hours post-exercise.

No significant differences in percent change from baseline 2 were noted between groups (P>0.05) for any biochemical or performance measure, with a trend noted for oxLDL (P=0.06) where values increased more with MSM compared to placebo, and total work on the Wingate cycle test (P=0.01) where values decreased slightly more with MSM (4.4%) compared to placebo (2.0%). A group effect was noted for the absolute change in muscle soreness during passive knee extensor stretching (P=0.0004), with values lower for MSM compared to placebo immediately post-exercise (2.5±0.4 *vs.* 3.0±0.5), 24 hours post-exercise (4.2±0.4 *vs.* 5.8±0.5), 48 hours post-exercise (4.4±0.6 *vs.* 5.8±0.5), and 72 hours post-exercise (2.5±0.6 *vs.* 4.0±0.5).

Discussion

This study aimed to determine the influence of MSM supplementation on oxidative stress, muscle soreness, muscle force produc-

tion and physical performance following eccentric knee extensor exercise in physically active men. Contrary to our hypothesis, MSM supplementation did not influence oxidative stress following eccentric exercise. Oxidative stress biomarkers were actually lower during the post-exercise period for both the MSM and placebo groups. Although 8-isoprostane values were lower for MSM compared to placebo at selected times post-exercise, differences were not significant. For example, values decreased from baseline 2 to 72 hours post exercise approximately 11% in the placebo group and 17% in the MSM group.

It was somewhat surprising that oxidative stress values decreased during the post exercise period — a finding that was consistent across all four variables assessed (using both blood and urine). Most prior studies have noted an increase in oxidative stress following eccentric exercise. For example, Sacheck *et al.*[30] reported a significant increase in plasma $F_{2\alpha}$-isoprostanes and MDA in young and old men after downhill running for 45 minutes at 75% VO_2max. Meydani *et al.*[31] also noted a significant elevation of urinary thiobarbituric acid levels following a single bout of downhill running at 75% of maximal heart rate for 45 minutes in young (+60%) and old (+80%) men. Similar findings have been observed in animals, as there is an increase in protein carbonyls in response to a single bout of eccentric exercise within skeletal muscle of rats.[32]

Contrary to the above, some authors have reported no increase in certain oxidative stress biomarkers following eccentric exercise. For example, Sacheck *et al.*[30] found that while eccentric exercise increased in plasma $F_{2\alpha}$-isoprostanes and MDA as indicated above, there was no significant change in leukocyte 8-hydroxy-2'-deoxyguanosine (8-OHdG). We have previously noted that plasma protein carbonyls and peroxides increased only slightly but failed to reach statistical significance following eccentric exercise.[33] The blunted response of oxidative stress may be driven by an enhanced antioxidant defense system because of a chronic exercise training adaptation. It is well accepted that regular exercise training improves antioxidant capacity and the oxidative damage repair systems, which possibly counteract oxidative stress, stimulating the repair process in response to certain stressful condition (*i.e.*, acute exercise).[34] The participants in the present study had a history of performing resistance exercise, which may have resulted in a blunted oxidative stress response following the eccentric exercise. In agreement with this assertion, Ramel et al. reported attenuating in lipid peroxidation in trained men following resistance exercise as compared to untrained subjects.[35] This agrees with findings from our past studies that show minor changes in protein carbonyl and MDA in response to a single bout of exercise in those who regularly exercise.[36, 37]

It should be noted that oxidative stress markers in the present study were only analyzed in blood (and urine with regards to 8-isoprostanes). It is possible that oxidative stress may have been elevated in skeletal muscle. Our inability to include skeletal muscle samples for analysis may be considered a limitation of this work, as the inclusion of muscle samples would have provided another tissue for comparing the oxidative stress response to eccentric exercise between MSM and placebo. In the present case, with no elevation noted in any variable, we cannot firmly conclude whether or not MSM is helpful to alleviate exercise-induced oxidative stress. We can simply note that MSM appears unnecessary for this purpose, as oxidative stress was not elevated in healthy, physically active men in the present study. The use of untrained, highly trained, and/or unhealthy individuals may have yielded differing findings.

Although significant interaction effects were not observed, it should be noted that from a practical perspective, muscle force was noted to recover more quickly with MSM treatment as compared to placebo (Table III). Of greatest importance, the MIF plateau remained 8% below baseline 2 values at 72 hours post-exercise in the placebo group, whereas this value was fully recovered in the MSM group at the same test time. While the importance of this finding requires further investigation, it may have im-

plications for individuals who train regularly and may benefit from a more rapid recovery to allow a return to intensive exercise. This may also have relevance to athletes who are required to generate force at high values within days of a competition (*e.g.*, rounds of competition in tournaments or championships). In fact, Myer *et al.*[38] reported that neuromuscular training for 7 weeks significantly enhanced hamstrings strength ($P<0.01$) and thus the muscle-related performance (*i.e.*, vertical jump) in high school female athletes. This group also reported that adolescent female athletes who participated in 6 weeks of neuromuscular training produced a remarkable increase in strength (1RM squat +92% and bench press 20%; $P<0.001$), and performance (0.07 s shorter (+38%) in 9.1-m sprint time; $P<0.001$) and this enhancement was accompanied with improved movement biomechanics, which may reduce injury risk in response to intense exercise.[39] In addition, Paavolainen *et al.*[40] reported positive effects of concurrent strength and aerobic training for 9 weeks on isometric force (+3.6-4.7%; $P<0.01$) accompanied with improvement of 5-km time ($P<0.05$) in endurance athletes. This finding supports the notion that greater muscle force may be associated with improved athletic performance. Hence, any improvement in muscle force recovery following high force exercise may prove beneficial with regards to overall physical performance. Of course, replication of the present experiment is necessary, perhaps utilizing a larger sample of subjects, and ideally observing a statistically significant effect for the noted measure.

Although not of statistical significance, muscle soreness (in particular during passive knee extensor stretching) was lower with MSM as compared to placebo (Table V). A reduction in soreness may allow individuals to return to regular training more quickly and/or perform training at a level where it will prove to be most productive. Ingram *et al.*[41] reported that young male athletes assigned to cold-water immersion treatment following intensive exercise showed reduced muscle soreness as compared to no treatment ($P<0.05$). In addition, the cold water treatment blunted the reduction in isometric muscle force (*i.e.*, leg extension and flexion) at 48 h post-exercise and facilitated a faster recovery of sprint performances to baseline level.[41] In agreement with their findings, Vaile *et al.*[42] also reported efficacy of specific water immersion treatment following exercise on facilitating a recovery of functional capacity associated with reduced muscle soreness. Collectively, it is plausible that specific soreness-reducing interventions (*i.e.*, MSM) can improve physiological and/or functional deficits related to muscle soreness in response to intense training, thus allowing individuals to return to regular training more quickly and/or participate in the training more actively with the result of optimal productivity.

Aside from MIF and muscle soreness, small but statistically insignificant improvements in performance with MSM treatment were noted in 20-yard sprint time and in treadmill run time. For example, 20-yard sprint time at 0 h post-exercise as compared to pre-exercise was 12% slower for placebo but only 7% slower for MSM. In regards to endurance performance, an increase in treadmill run time at 72 hours post-exercise was greater in the MSM group (+7%) than the placebo group (+2%). While difference failed to reach statistical significance, these data may suggest beneficial effects of MSM on enhancing post-exercise recovery and anaerobic and aerobic capacity; this improvement, as mentioned above, may be facilitated by the relief in muscle soreness and a more rapid recovery of muscle force production.

It should be noted that these findings are in reference to a sample of physically active men that regularly engage in structured resistance exercise. Such individuals are likely "protected" from excessive muscle injury due to the adaptations that are present as a result of performing regular exercise training.[43] It is possible that individuals who are not as well-trained may benefit from MSM supplementation to a greater degree, and if such individuals were used in the present design, it is very likely that results would have been more robust. That said, generalizing results obtained from an untrained subject group to those who regu-

lar perform strenuous exercise training would be problematic, and the repeated-bout effect would have to be considered.

Conclusions

Considering the available data, MSM supplementation in physically active men who perform high force eccentric exercise does not appear necessary for purposes of reducing oxidative stress (as little change occurs in oxidative stress biomarkers post-exercise). MSM appears to have some influence on muscle force recovery (as measured by MIF) and may attenuate muscle soreness during passive stretching. These findings may have relevance to individuals who are regularly engaged in strenuous exercise known to induce muscle injury.

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